# PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

## PCT

### NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

| | |
|---|---|
| **Date of mailing** (day/month/year)<br>29 January 2001 (29.01.01) | |
| **International application No.**<br>PCT/GB00/02217 | **Applicant's or agent's file reference**<br>PBA/D88421PWO |
| **International filing date** (day/month/year)<br>19 June 2000 (19.06.00) | **Priority date** (day/month/year)<br>19 June 1999 (19.06.99) |
| **Applicant**<br>BARBER, Jill et al | |

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

08 December 2000 (08.12.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

| | |
|---|---|
| **The International Bureau of WIPO**<br>**34, chemin des Colombettes**<br>**1211 Geneva 20, Switzerland** | Authorized officer<br>Olivia TEFY |
| Facsimile No.: (41-22) 740.14.35 | Telephone No.: (41-22) 338.83.38 |

# PATENT COOPERATION TREATY

# PCT



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| PBA/0088421PWO | | |
| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
| PCT/GB00/02217 | 19/06/2000 | 19/06/1999 |
| International Patent Classification (IPC) or national classification and IPC<br>C07H17/00 | | |
| Applicant<br>THE VICTORIA UNIVERSITY OF MANCHESTER et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 08/12/2000 | 15.11.2001 |
| Name and mailing address of the international preliminary examining authority:<br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized officer<br>Hornich, E<br>Telephone No. +49 89 2399 8721 |

Form PCT/IPEA/409 (cover sheet) (January 1994)

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02217

## I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
**Description, pages:**

1-18 as originally filed

**Claims, No.:**

1-17 as originally filed

**Drawings, sheets:**

1/24-24/24 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-8, 14-17 partly (see Section III, 1.); 15, 17.

because:

☒ the said international application, or the said claims Nos. 15, 17 (with regard to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*): **see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-8, 14-17 (partly).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N) Yes: Claims 1-9, 12, 17

| | | | |
|---|---|---|---|
| | No: | Claims | 10, 11, 13-16 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-9, 12, 17 |
| Industrial applicability (IA) | Yes: | Claims | 1-14, 16 |
| | No: | Claims | |

2. Citations and explanations
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
**see separate sheet**

## SECTION III

1. The IPEA will only formulate an assessment of novelty, inventive step and industrial applicability for the *parts of the present claims for which an International Search Report has been drawn up* (**R. 66.1(e) PCT**) (cf. form PCT/ISA/210, Box I), i.e. only for *those parts relating to the compounds mentioned in claims 9, 10, 11 and 12 (Erythromycin B, 2'-esters of Erythromycin B, enol ethers of Erythromycin B;* the compounds and in relation to microbial infection), i.e. for ***claims 1-8 and 14-17 partly*** (see also **Section VIII**).

2. Claims 15 and 17 relate to subject-matter considered by this Authority to be covered by the provisions of **R. 67.1(iv) PCT**. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (**Art. 34(4)(a)(i) PCT**).

## SECTION V

3. *References*:

**D1**: MARTIN, YVONNE C. ET AL: 'Chemical modification of erythromycin antibiotics. 4. Structure-activity relations of erythromycin esters' J. MED. CHEM. (1972), 15(6), 635-8.

**D2**: OMURA, SADAFUMI ET AL: 'Research and development of clarithromycin' YAKUGAKU ZASSHI (1992), 112(9), 593-614.

**D3**: JONES, PETER H. ET AL: 'Chemical modifications of erythromycin antibiotics. 3. Synthesis of 4" and 11 esters of erythromycin A and B' J. MED. CHEM. (1972), 15(6), 631-4.

**D4**: ONO, HIDEO ET AL: 'Drug resistance in Staphylococcus aureus. Induction of macrolide resistance by erythromycin, oleandomycin, and their derivatives' JPN. J. MICROBIOL. (1975), 19(5), 343-7.

**D5**: BOJARSKA-DAHLIG, HALINA ET AL: 'Quantitative structure-activity relationships in erythromycin group with MTD technique' POL. J. PHARMACOL. PHARM. (1981), 33(3), 359-63.

**D6**: KIBWAGE I O ET AL: 'ANTIBACTERIAL ACTIVITIES OF ERYTHROMYCINS

A B C AND D AND SOME OF THEIR DERIVATIVES' ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 28, no. 5, 1985, pages 630-633, ISSN: 0066-4804.

**D7**: CANE, DAVID E. ET AL: 'Macrolide biosynthesis. 3. Stereochemistry of the chain-elongation steps of erythromycin biosynthesis' J. AM. CHEM. SOC. (1986), 108(16), 4957-64.

**D8**: EP-A-0 553 353

**D9**: MORDI, MOHD N. ET AL.: 'Acid-Catalyzed Degradation of Clarithromycin and Erythromycin B: A Comparative Study Using NMR Spectroscopy' J. MED. CHEM. , vol. 43, no. 3, 2000, pages 467-474.

**D10**: BOJARSKA-DAHLIG, H.: 'Correlation of physicochemical parameters and antibacterial activity of macrocyclic antibiotics' ABH. AKAD. WISS. DDR, ABT. MATH., NATURWISS., TECH. (1978), (2N, QUANT. STRUCT.-ACT. ANAL.), 343-9.

**D9** was *published between the priority date and the filing date* of the present application and has *not been considered relevant prior art*, as the examination has been carried out ***on the assumption*** that the ***priority has been validly claimed.***

4. *Novelty* **(Art. 33(2) PCT)** ***with regard to item 1.***

4.1 **D1** to **D8** and **D10** disclose *Erythromycin B* (e.g. **D2**, table II; **D4**), *2'-esters* thereof (e.g. formyl-, acetyl-, propionyl-, benzoate (**D7**), ethyl succinate (**D8**, see further **D1**, **D3**, **D10**)) and *Erythromycin B enol ether* (**D5**, p. 363, l. 4/5) and report on the *antimicrobial activity* of the compounds.

Thus, as *2'-esters of Erythromycin B* with mono- or dicarboxylic acids and *Erythromycin B enol ether* have already been disclosed, the subject-matter of claims 10, 11 and 13 can**not** be regarded **novel**.

4.2 **D6** discloses that commercially available samples of Erythromycin also comprise *Erythromycin B and Erythromycin enol ether* (Erythromycin B present up to 13%; '*the European Pharmacopoeia now has a limit of about 5% for these related substances*'; see p. 630, left col., paragraph 1; p. 632, right col., paragraph 3).

As (those commercially available samples of) Erythromycin is/are commonly used for the treatment of *bacterial infections*, *Erythromycin B and the enol ether have implicitly been used in medical treatment* (as comprised in the samples).
The *2'-esters of Erythromycin B* (e.g. ethylsuccinate) disclosed within **D8** show relieved bitterness compared to Erythromycin when *orally administered* (bacterial infections; ex. 10; p. 8, last paragraph).

Therefore, *Erythromycin B, the enol ether and 2'-esters of Erythromycin B* have already been used in the treatment of bacterial infections; thus, **D8** and **D10** **anticipate** the subject-matter of claims 14-16.

4.3 The subject-matter of claims 1-9, 12 and 17 appears to be **novel**, as neither the *succinate of Erythromycin B* nor compositions comprising *at least 50%* or particular amounts (as defined in claims 5 and 6) of Erythromycin B have been disclosed (with regard to item 1.).

5. *Inventive Step* **(Art. 33(3) PCT)** ***with regard to item 1.***

5.1 The object (problem to be solved in) of the present application is to provide *alternative antibacterial agents to Erythromycin A, clarithromycin and azithromycin* in order to obviate or mitigate the disadvantages associated with the above-mentioned antibiotics (e.g. side effects due to degradation products).

The *solution* of the present application resides in the provision of *Erythromycin B* and *2'-esters of Erythromycin B* or *Erythromycin B enol ether* and pharmaceutical compositions comprising the compounds in defined amounts (for the treatment of microbial infections).

*Erythromycin B* and other related compounds, e.g. the *enol ether*, are comprised in commercially available samples of Erythromycin (**D6**). The *antimicrobial activity* of *Erythromycin B* and derivatives (2'-esters) has been investigated and is known from **D1** to **D10** (see 'novelty'). *Erythromycin B 2'-esters* have already been used due to their alleviated bitterness and improved bioabsorbability (**D8**).

The *difference* between the prior art and the present application appears to be the *amount* of Erythromycin B or derivative comprised in the composition, respectively the particular derivative *succinate ester*.

However, the application does not contain any data showing the *effect* of the particular amount of '*at least 50%*' or the particular derivative '*succinate ester*'.

Thus, as the claimed effect has not been evidenced, an **inventive step** could presently **not be acknowledged** for the subject-matter of claims 1-9, 12 and 17.

6. *Industrial Applicability* **(Art. 33(4) PCT)**

6.1 The requirements of industrial applicability appear to be fulfilled for claims 1-13.

6.2 For the assessment of the present claims 14-17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**SECTION VIII**

7. '*Derivative of Erythromycin B*' (claims 1-6, 14-16 and also the dependent claims 7 and 17) does not refer to a well-defined group of compounds, thus leaving doubts about the components being encompassed by this definition.
Thus, the above-mentioned claims *lack clarity* in the sense of **Art. 6 PCT**.

8. Concerning claim 10, it is not clear if *Erythromycin B enol ether* itself or *2'-esters of* Erythromycin B enol ether should be within the scope of protection (with regard to the subject-matter of claim 9) **(Art. 6 PCT)**.

9. The *category* of claim 17 as referring to '*a use or a method*' is not clear **(Art. 6 PCT)**.

PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference | FOR FURTHER ACTION | see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |
|---|---|---|
| PBA/D88421PWO | | |
| International application No. | International filing date *(day/month/year)* | (Earliest) Priority Date *(day/month/year)* |
| PCT/GB 00/ 02217 | 19/06/2000 | 19/06/1999 |

Applicant

THE VICTORIA UNIVERSITY OF MANCHESTER

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[X] None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

In view of the wording of claims 1-11,13-17 presently on file, in as far as the expression "Pharmaceutically acceptable derivative of Erythromycin B, enol ether of Erythromycin B" is concerned, which renders it difficult, if not impossible, to determine the matter for which protection is sought, the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful search is impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and concise), namely the compositions/uses devices comprising Erythromycin B, 2'-esters of erythromycin, and internal enol ethers of Erythromycin B.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/02217

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61P31/00 A61K31/7048 C07H17/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, BIOSIS, EPO-Internal, EMBASE, WPI Data, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | MARTIN, YVONNE C. ET AL: "Chemical modification of erythromycin antibiotics. 4. Structure-activity relations of erythromycin esters" J. MED. CHEM. (1972), 15(6), 635-8 , XP001024313 the whole document --- | 1-11, 13-17 |
| X | OMURA, SADAFUMI ET AL: "Research and development of clarithromycin" YAKUGAKU ZASSHI (1992), 112(9), 593-614 , XP002096748 abstract; tables 2,6 --- -/-- | 1-8, 14-17 |

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 27 September 2001 | 12/10/2001 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | A. Jakobs |

4

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication,where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | JONES, PETER H. ET AL: "Chemical modifications of erythromycin antibiotics. 3. Synthesis of 4'' and 11 esters of erythromycin A and B" J. MED. CHEM. (1972), 15(6), 631-4 , XP002178020 abstract page 633, column 2, paragraph 13 -page 634, column 1, paragraph 6 --- | 10,11 |
| X | ONO, HIDEO ET AL: "Drug resistance in Staphylococcus aureus. Induction of macrolide resistance by erythromycin, oleandomycin, and their derivatives" JPN. J. MICROBIOL. (1975), 19(5), 343-7 , XP001028153 abstract; table 2 --- | 1-8, 14-17 |
| X | BOJARSKA-DAHLIG, HALINA ET AL: "Quantitative structure-activity relationships in erythromycin group with MTD technique" POL. J. PHARMACOL. PHARM. (1981), 33(3), 359-63 , XP001028146 abstract page 359; table 1 --- | 1-8, 14-17 |
| X | KIBWAGE I O ET AL: "ANTIBACTERIAL ACTIVITIES OF ERYTHROMYCINS A B C AND D AND SOME OF THEIR DERIVATIVES" ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 28, no. 5, 1985, pages 630-633, XP001028634 ISSN: 0066-4804 the whole document --- | 1-8, 14-17 |
| X | CANE, DAVID E. ET AL: "Macrolide biosynthesis. 3. Stereochemistry of the chain-elongation steps of erythromycin biosynthesis" J. AM. CHEM. SOC. (1986), 108(16), 4957-64 , XP002178022 abstract page 4959, column 2, paragraph 3 --- | 10,11 |
| X | EP 0 553 353 A (TAISHO PHARMA CO LTD) 4 August 1993 (1993-08-04) abstract; claims 1,2; example 10 --- -/-- | 10 |

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| P,X | MORDI, MOHD N. ET AL.: "Acid-Catalyzed Degradation of Clarithromycin and Erythromycin B: A Comparative Study Using NMR Spectroscopy" J. MED. CHEM. , vol. 43, no. 3, 2000, pages 467-474, XP001028101 the whole document | 1-17 |
| X | BOJARSKA-DAHLIG, H.: "Correlation of physicochemical parameters and antibacterial activity of macrocyclic antibiotics" ABH. AKAD. WISS. DDR, ABT. MATH., NATURWISS., TECH. (1978), (2N, QUANT. STRUCT.-ACT. ANAL.), 343-9 , XP001028142 abstract page 345, paragraph 6 -page 346, paragraph 1; table 1 | 1-8, 14-17 |
| X | NATL COORD GROUP INVEST SHORT-COURSE CHEMOTHER: "SHORT COURSE CHEMO THERAPY IN PULMONARY TUBERCULOSIS." CHIN J TUBERC RESPIR DIS, (1982) 5 (2), 78-81. , XP001028067 the whole document | 1-8, 14-17 |
| X | WO 98 33482 A (ABBOTT LAB) 6 August 1998 (1998-08-06) abstract; claim 9 page 1, line 8-30 | 1-8, 14-17 |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 00/02217

| Patent document cited in search report | | Publication date | Patent family member(s) | | Publication date |
|---|---|---|---|---|---|
| EP 0553353 | A | 04-08-1993 | EP | 0553353 A1 | 04-08-1993 |
| | | | WO | 9206991 A1 | 30-04-1992 |
| | | | US | 5350839 A | 27-09-1994 |
| WO 9833482 | A | 06-08-1998 | AU | 6041498 A | 25-08-1998 |
| | | | EP | 0975330 A1 | 02-02-2000 |
| | | | WO | 9833482 A1 | 06-08-1998 |
| | | | ZA | 9800833 A | 26-05-1999 |